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TECHNOLOGY

Computer Models Help Speed The Search for Useful Drugs

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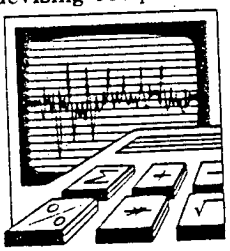
DRUG RESEARCH takes the same combination of persistence and luck as panning for gold. Pharmaceutical companies typically test more than 20,000 compounds to sift out one marketable drug, and most drug researchers never find anything salable.

But now computers are improving the odds by speeding up almost every phase of drug development—from devising recipes for new substances to clinical testing. One of the most important advances involves the visualization of complex molecules with sophisticated computer graphics. The visualizations, which sometimes look like an explosion in a tinker-toy factory, help scientists predict drugs' effects. Researchers are beginning to use such information to tailor more potent drugs with fewer side effects.



"Traditionally, we try to stumble onto something useful, then gradually refine it," says T.J. O'Donnell, a drug researcher with Abbott Laboratories. With the new computerized techniques, he says, "we can truly design things."

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THE METHOD has its problems, though. Receptors tend to be large, floppy protein molecules that constantly change shape. Most receptors' shapes simply aren't known. And electrical attraction and repulsion between receptor and drug molecules, among other things, complicate the binding process. More precise calculations made with supercomputers can solve some of these problems, but "you could take the entire computing power of the CIA and bring it to its knees without getting anywhere on many problems," says Garland Marshall, a biophysics professor at Washington University in St. Louis, who uses molecular modeling in research on receptor sites.

Once drug researchers identify molecules of interest, they often are faced with the difficult task of making them in the test tube. A number of computer programs have been developed to help with this problem, but only recently have they become sophisticated enough to be of much use in drug research.

Most of the programs work backward from a desired end-product, searching a database of simpler molecules that will react to produce it. Drug companies recently have formed consortia to expand the databases of such programs.

Promising as the programs are, however, they aren't going to make chemists obsolete. Says Alan Long, a Harvard University chemist who has helped develop a widely used synthesis program, "You can calculate ways to do things all day long with the computer, and Mother Nature will just thumb her nose at you when you try them in the lab."

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